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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,681	08/18/2003	Orville G. Kolterman	254/057CON	4614

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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
07/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,681	KOLTERMAN ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/24/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-30 and 38-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-30, and 38-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice of Non-compliant Amdt.*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/24/07 has been entered.

Claim Status

2. Claims 1-23, 31-37, and 60-69 have been cancelled.

Claims 24-30, and 38-59 are currently pending.

Claims 24-30 and 38-59 are being examined in this application.

Non-Complaint Claim Amendments

3. The claim amendment filed on 4/24/07 is not in compliance 37 CFR 1.121. See the attached "Notice of Non-complaint Amendment" for details.

Election/Restriction

4. Applicant's election with traverse of 25,28,29 tri-pro human amylin as the elected species in the correspondence dated 10/29/04 is as previously acknowledged and was previously made final.

Priority

5. This application is a CONTINUATION of U.S. Patent Application No. 09/576,062 (filed 5/22/2000), which is now a US PATENT, 6,608,029 (8/19/2003). The U.S. Patent Application No. 09/576,062 is a CONTINUATION of U.S. Patent Application Nos. 08/302,069 (filed 9/7/1994), which is now a US PATENT, 6,114,304 (9/5/2000). The U.S. Patent Application No. 08/302,069 is a CIP of U.S. Patent Application Nos. 08/118,381 (filed 9/7/1993), which is now abandoned.

Claim Objection(s) / Rejections Withdrawn

6. In light of the new rejections, the following claim objection is withdrawn:

Claims 25-30, and 41-59 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Outstanding Objection(s) and/or Rejection (s)

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 24 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Sarantakis et al (US 4,451,394; 05/29/1984; cited previously). The previous rejection is

maintained for the reasons of record as set forth in the Office action, mailed 7/3/06, at p. 6+.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the added limitation of "binds to an amylin receptor" is not taught by the cited reference. (Reply. pp. 9-10, bridging para). Applicants also argue that the reference is "silent with regard to amylin, amylin analogs and amylin receptors". (Reply, p. 10, para 2).

As discussed in the previous rejection, the term "amylin agonist analogue" is broadly defined to encompass almost any peptide.

The instant specification defines the term "amylin agonists" as "refers to compounds which mimic the effects of amylin". (Spec. p. 13, para 3). The instant specification also defines the term "amylin agonist analogue" as "derivatives of an amylin which act as amylin agonists, normally, it is presently believed, by virtue of binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which amylin itself may interact to elicit those biological properties ..." (Spec. p. 13, para 3). The instant specification also states "amylin itself and amylin agonist analogue may also be referred to broadly as amylin agonists." (Spec. 13, para 3). Thus, the term "amlyin agonist analogue" broadly refers to any compound

that "mimics amylin", by "direct or indirectly" interacts with "an amylin receptor" or "other receptor".

The instant specification also does not specifically define the term "amylin receptor". The relevant passage in the instant specification states "amylin agonist analogue" as "derivatives of an amylin which act as amylin agonists, normally, it is presently believed, by virtue of binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which amylin itself may interact to elicit those biological properties ..." (Spec. p. 13, para 3). That is an "amylin receptor" can be almost any receptor that is "directly" or "indirectly" interact with amylin, which "receptor" would broadly encompass at least any receptor in the metabolic pathway.

Furthermore, as discussed below, the term "binds" is not clearly defined by either the instant claims or the specification. The term can encompass low affinity binding, or non-specific binding.

The '394 patent teaches a peptide that are used for treatment of postprandial blood glucose levels. In order for peptide drug to exert their effects, the peptides must be uptaken by the cells. This "uptake" is usually through the action of cell receptors (i.e. binding to the receptor), as evidenced by El-Andaloussi et al (Current Pharmaceutical Design. Vol. 11: 3597-3611; 2005; p. 3597, col.1, para 1, bottom; p. 3597, col.2, para 2). Thus, the reference inherently teaches that the dodecapeptide can bind to a receptor, which can be an amylin receptor, as broadly defined by the instant specification.

Applicants have not demonstrated how the reference's peptide is structurally and/or functionally different from the "amylin agonist analogues" of the instant claims. Thus, the reference's teaching anticipates the instantly claimed invention.

New Claim Objection(s) and Rejection(s)

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

11. Claims 24 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal an amylin or an amylin agonist analogue in an amount effective to reduce or moderate a postprandial rise in plasma glucose, wherein the amylin agonist analogue is a peptide and binds to an amylin receptor.

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in

possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398; 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant claims (especially Claim 24) are drawn to a genus of methods of therapeutic treatment using amylin or "amylin agonist analogues". The instant claim (24) is drawn to using any "amylin agonist analogue" for treatment of "reduce or moderate a postprandial rise in plasma glucose" in any mammal (including human). The instant specification defines the term "amylin agonists" as "refers to compounds which mimic the effects of amylin". (Spec. p. 13, para 3). The instant specification also defines the term "amylin agonist analogue" as "derivatives of an amylin which act as amylin agonists, normally, it is presently believed, by virtue of binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which

amylin itself may interact to elicit those biological properties ..." (Spec. p. 13, para 3). The instant specification also states "amylin itself and amylin agonist analogue may also be referred to broadly as amylin agonists." (Spec. 13, para 3). Thus, the term "amlyin agonist analogue" broadly refers to any compound that "mimics amylin", by "direct or indirectly" interacts with "an amylin receptor" or "other receptor". That is the claimed "amylin agonist analogue" can be any compound (peptide) that interacts with almost any receptor.

Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "amylin agonist analogues" that is a peptide and binds to a receptor, and can be used for treatment of lowing blood glucose. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of "amyloid agonist analogues".

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the only examples of "amylin agonist analogues" are the ones listed in the instant claims (e.g. Claims 25-30), and the ones listed in the Examples of the instant specification (e.g. pp. 42+). However, the instant claims are drawn to any peptide that binds to an amylin receptor.

The structure and its corresponding function (or property) for "amylin" is highly unpredictable. For example, Pittner et al (Journal of Cellular Biocheistry. Vol. 55S: 19-28; 1994; 1 year later than the instant earliest claimed priority data), state the followings:

"In human amylin the reigon between amino acids 20 and 29 appears to form beta-pleated sheets and to be responsible for the very strong tendency to self-aggregate and form the insoluble plaques, which are pancreatic amyloid material [5]. This feature makes human amylin extremely difficult to work with either as an experimental tool or as a potential therapeutic agent." (emphasis added; pp. 19-20, bridging para)

Thus, even the structure and the corresponding property (such as blood glucose reducing function) of "amylin" itself is highly unpredictable. That is it is highly unpredictable how an "amylin" when administered to human or other animals would "effectively" "reduce or moderate a postprandial rise in plasma glucose", as instantly claimed. Further, the broadly encompassing term "amylin agonist analogue" peptide would drawn to a peptide that is different or the same as "amylin" itself as defined by the instant specification. However, it is not known that all "peptides" that bind to a so-called "amylin receptor" has the property of lowering blood glucose and thus can be used as a therapeutic agent. For example, $^{8-37}$h-CGRP taught by Wang et al (FEBS. Vol. 291 (2): 195-198; 1991; cited in IDS) has similar amino acid sequence as the human amylin (see Figure 1 of the reference), and would be encompassed by the broad definition for the term "amylin agonist analog", as defined in the instant specification. Wang et al, teach the $^{8-37}$h-CGRP has similar amino acid sequences as the "human amylin", and it binds to an "amylin receptor" (pp. 195-196, bridging para). Thus, the $^{8-37}$h-CGRP "mimics the effects of", or "act as amylin agonists, normally, it is presently believed, by virtue of

binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which amylin itself may interact to elicit those biological properties ..." (as defined by the instant specification). However, the $^{8-37}$h-CGRP peptide does not has the property of "reduce or moderate a postprandial rise in plasma glucose". In fact, the Wang reference states $^{8-37}$h-CGRP is an "antagonist" to the amylin receptor, and it "antagonize" the action of "amylin" itself (Abstract; Figures 3-4).

Thus, it is highly unpredictable which "peptide" that binds to a so-called amylin receptor would possess the desired "agnostic" effects when administered to a human or an animal.

Furthermore, Edwards et al (Life Sciences. Vol.51:1899-1912; 1992), throughout the reference reviews the function and structure of "Amylin" (Abstract). The Edward reference states Amylin function to "inhibiting insulin stimulated glucose metabolism, decreasing glucose clearance" (p. 1905, 2nd to last para). Thus, Amylin functions to increase blood glucose as shown by the state of the art at the time of the invention was made, but not reduction in blood glucose as instantly claimed. The prior art's teaching indicates that using amylin itself to reduce blood glucose level is highly unpredictable.

In addition, the term "amylin receptor" is broad and encompasses various known and unknown receptors, whose structures and/or functions are not well understood. For examples, Pittner et al (citation omitted) teach a distinct and specific "amylin receptor" is not known (p. 24, col.1, para 2). As instantly claimed, an "amylin agonist analogue" is a peptide that binds to "an amylin receptor". Thus, the possession of an amylin receptor, and an (screening) assay for identifying a peptide that binds to the receptor must be

demonstrated. Without the possession of the claimed "amylin receptor", the peptide "amylin agonist analogue" would not be identified, and thus not in possession.

In addition, the case laws have addressed the issues of written description for methods using compounds that are yet to be identified.

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."
>
> MPEP 2163. (emphasis added).

In this case, neither the instant specification nor the claims provided any specific structural limitation for the broadly claimed "amylin agonist analogue". The instant specification at best only describes "a wish or plan for obtaining" a peptide that bidns to "an amylin receptor" and would be used for therapeutic effects. Similar to the Rochester case, the instant disclosure has not demonstrated possession of the entire claimed genus of "amylin agonist analogues", and the genus of methods for treatment of using the amylin agonist analogues. Applicant's claimed scope represents only an invitation to experiment regarding possible peptides that would possession the required properties and/or structures.

The recited method of reducing blood glucose is essentially a trial and error process that would involve identifying peptides that can act as "amylin agonist analogue" by binding to "an amylin receptor" and effective reduce blood glucose postprandially after administering. Without identifying the required peptides that have the required properties and/or structures, the claimed method of treatment cannot be accomplished.

Therefore, applicants are not in possession of the claimed entire genus of "amylin agonist analogues", and the entire genus of methods of treatment.

Scope of Enablement Rejection

12. Claims 24 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treatment of reducing postprandial rise in blood glucose using peptides with SEQ ID Nos: 1, 3, 6, 8-10, 31, 38 and 41-49, does not reasonably provide enablement for using any other peptides that binds to an amylin receptor for treatment of blood glucose levels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;

6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims / The nature of the invention

The nature of the invention (Claim 24) is a method of treating postprandial rise in blood glucose level using "amylin agonist analogues" in human and animals. The breadth of the claims seems to encompass a genus of methods of therapeutic treatment using amylin or "amylin agonist analogues". The instant claim (24) is drawn to using any "amylin agonist analogue" for treatment of "reduce or moderate a postprandial rise in plasma glucose" in any mammal (including human). The instant specification defines the term "amylin agonists" as "refers to compounds which mimic the effects of amylin". (Spec. p. 13, para 3). The instant specification also defines the term "amylin agonist analogue" as "derivatives of an amylin which act as amylin agonists, normally, it is presently believed, by virtue of binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which amylin itself may interact to elicit those biological properties ..." (Spec. p. 13, para 3). The instant specification also states "amylin itself and amylin agonist analogue may also be referred to broadly as amylin agonists." (Spec. 13, para 3). Thus, the term "amlyin agonist analogue" broadly refers to any compound that "mimics amylin", by "direct or indirectly" interacts with "an amylin receptor" or "other receptor". That is the claimed "amylin agonist analogue" can be any compound (peptide) that interacts with almost any receptor.

The state of the prior art/ The predictability or lack thereof in the art

The structure and its corresponding function (or property) for "amylin" is highly unpredictable. For example, Pittner et al (Journal of Cellular Biocheistry. Vol. 55S: 19-28; 1994; 1 year later than the instant earliest claimed priority data), state the followings:

"In human amylin the reigon between amino acids 20 and 29 appears to form beta-pleated sheets and to be responsible for the very strong tendency to self-aggregate and form the insoluble plaques, which are pancreatic amyloid material [5]. This feature makes human amylin extremely difficult to work with either as an experimental tool or as a potential therapeutic agent." (emphasis added; pp. 19-20, bridging para)

Thus, even the structure and the corresponding property (such as blood glucose reducing function) of "amylin" itself is highly unpredictable. That is it is highly unpredictable how an "amylin", when administered to human or other animals, would "effectively" "reduce or moderate a postprandial rise in plasma glucose", as instantly claimed. Further, the broadly encompassing term "amylin agonist analogue" peptide would drawn to a peptide that is different or the same as "amylin" itself as defined by the instant specification. However, it is not known that all "peptides" that bind to a so-called "amylin receptor" has the property of lowering blood glucose and thus can be used as a therapeutic agent. For example, $^{8-37}$h-CGRP taught by Wang et al (FEBS. Vol. 291 (2): 195-198; 1991) has similar amino acid sequence as the human amylin (see Figure 1 of the reference), and would be encompassed by the broad definition for the term "amylin agonist analog" of the instant specification. Wang et al, teach the $^{8-37}$h-CGRP has similar amino acid sequences as the "human amylin", and it binds to an "amylin receptor" (pp. 195-196, bridging para). Thus, the $^{8-37}$h-CGRP "mimics the effects of", or "act as amylin

agonists, normally, it is presently believed, by virtue of binding to or other wise directly or indirectly interacting with an amylin receptor or other receptor or receptors with which amylin itself may interact to elicit those biological properties ..." (as defined by the instant specification). However, the $^{8-37}$h-CGRP peptide does not has the property of "reduce or moderate a postprandial rise in plasma glucose". In fact, the Wang reference states $^{8-37}$h-CGRP is an "antagonist" to the amylin receptor, and it "antagonizes" the action of "amylin" itself (Abstract; Figures 3-4).

Thus, it is highly unpredictable which "peptide" that binds to a so-called amylin receptor would possess the desired "agnostic" effects when administered to a human or an animal.

Furthermore, Edwards et al (Life Sciences. Vol.51:1899-1912; 1992), throughout the reference reviews the function and structure of "Amylin" (Abstract). The Edward reference states Amylin function to "inhibiting insulin stimulated glucose metabolism, decreasing glucose clearance" (p. 1905, 2nd to last para). Thus, Amylin functions to increase blood glucose as shown by the state of the art at the time of the invention was made, but not reduction in blood glucose as instantly claimed. The prior art's teaching indicates that using amylin itself to reduce blood glucose level is highly unpredictable.

In addition, the term "amylin receptor" is broad and encompasses various known and unknown receptors, whose structures and/or functions are not well understood. For examples, Pittner et al (citation omitted) teach a distinct and specific "amylin receptor" is not known (p. 24, col.1, para 2). As instantly claimed, an "amylin agonist analogue" is a peptide that binds to "an amylin receptor". Thus, assays for identifying a peptide (that is

an amylin agonist) would be highly unpredictable because not all the so-called "amylin receptors" are known.

The above discussion only illustrated a few problems with using various peptides for treatment. Although there may be suggested methods of overcoming these problems through non-routine experimentations, there are no predictable methods or solutions that would solve all the problems for any peptides that are broadly encompassed by the instant definition.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D./MD level.

The amount of direction or guidance present / The presence or absence of working examples

The only guidance present in the instant specification is directed to generating "amylin agonist analogues" with certain peptide sequences (e.g. SEQ ID Nos 41-49), and treatment blood glucose level postprandially using the "tripro-amylin (AC-0137)" in human (e.g. pp. 35+, Example 4). There is no guidance described for using other peptides that are any derivatives of the wildtype "amylin" to treat postprandial blood glucose level. In addition, there is also no guidance to describe making any other peptides that have any structure to possess the function of amylin receptor binding property and blood glucose lowering properties.

The quantity of experimentation needed

Due to the unpredictabilities of peptides with various amino acid sequences to bind to "an amylin receptor" while exerting postprandial blood glucose lowering property in human and animals, as well as the unpredictability of making amylin receptor binding peptides that has the property of lowering postprandial blood glucose, undue experimentation would be required. As discussed above, the art has shown that not all amylin derivatives (i.e. any mutants of amylin) or analogues (any peptide with one of amylin's properties) can be used as an amylin agonist to reduce postprandial blood glucose level. The art also state that not all of the amylin receptors are identified and characterized. Thus, identifying "amylin agonist analogue" based on its binding to an amylin receptor is also highly unpredictable. Because the instant specification only provides guidance for a few examples of treatment using one amylin analogue (or structurally similar peptides with defined mutations), undue experimentation would be required to practice claimed method of using any peptides that bind to "an amylin receptor".

Conclusion

Due to the non-routine experimentation necessary to determine the specific methods for generating the desired "amylin agonist analogues", and the methods for treating postprandial blood glucose levels using the amylin agonist analogues; the lack of direction/guidance presented in the specification regarding the specific requirements for the method; the unpredictability of the methods as established by the state of the prior art; the breadth of the claims, undue experimentation would be required of a skilled artisan to make and/or use the claimed invention in its full scope.

Second paragraph of 35 U.S.C. 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 24-30 and 38-59 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is amended to recite the phrase "binds to an amylin receptor", which the term "binds" is indefinite. The term "binds" in is a relative term which renders the claim indefinite. The term "binds" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear from neither the instant specification nor the claims what degree of binding or what structures are required for a peptide to be an amylin agonist analogue, and additionally for the peptide to exhibit the instantly claimed therapeutic effects.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
6/27/07

/Jon D. Epperson/
Primary Examiner, AU 1639

Notice of Non-Compliant Amendment (37 CFR 1.121)	Application No. 10/643,681	Applicant(s) KOLTERMAN ET AL.	
	Examiner Sue Liu	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The amendment document filed on 4/24/07 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121 or 1.4. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
  - ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other _____.
- ☐ 2. Abstract:
  - ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other _____.
- ☐ 3. Amendments to the drawings:
  - ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other _____.
- ☒ 4. Amendments to the claims:
  - ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☒ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☒ E. Other: *See Continuation Sheet*.
- ☐ 5. Other (e.g., the amendment is unsigned or not signed in accordance with 37 CFR 1.4):

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For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714.

TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:

1. Applicant is given **no new time period** if the non-compliant amendment is an after-final amendment or an amendment filed after allowance. If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted.

2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the correction, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a *Quayle* action. If any of above boxes 1. to 4. are checked, the correction required is only the **corrected section** of the non-compliant amendment in compliance with 37 CFR 1.121.

   Extensions of time are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.

   Failure to timely respond to this notice will result in:
   Abandonment of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or
   Non-entry of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.

_____ _____

Legal Instruments Examiner (LIE), if applicable Telephone No.

Continuation of 4(e) Other: Claims 25-30 and 56 recite specific SEQ ID NOs as previously filed (4/10/06), but the SEQ ID NOs are removed from the amended claims filed on 4/27/07. The amended claims are not identified by the right claims status identifiers and the text do not contain appropriate markings to indicate alterations to the claims.